Tumorigenic effects of dichloroacetic acid in female F344 rats

Charles E. Wood[1], Dennis E. House[1], Michael H. George[1], Stephen Kilburn[1], Tanya M. Moore[1], Anthony B. DeAngelo[1]

[1] National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC

Corresponding author: Charles E. Wood, National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, B105-03, 109 T.W. Alexander Drive, Research Triangle Park, NC 27711, USA, Email: wood.charles@epa.gov

Introduction: Dichloroacetic acid (DCA) is a halogenated organic acid produced during oxidant disinfection of drinking water. Prior studies indicate that DCA may increase liver tumors in mice. Here we evaluated the hepatic tumorigenicity of DCA in female rats when given alone or prior to phenobarbital (PB), a liver tumor promoter in rodents.

Methods: This study followed a stop-promotion design in which female F344 rats were divided into six treatment groups: (1) deionized water (dH_2O, control); (2) dH_2O switching to PB at 4 weeks; (3) DCA (1.0g/L); (4) DCA (1.5g/L) switching to dH_2O at 4 weeks; (5) DCA (1.5g/L) switching to PB at 4 weeks; and (6) DCA (1.0g/L) switching to dH_2O at 26 weeks (n=40-60/group). Treatment lasted for 100 weeks with interim pathology evaluations at week 52 (n=10/group for groups 1-5).

Results: No significant treatment-related effects on tumor incidence were observed for liver, adrenal gland, pituitary gland, uterus, or thyroid gland. Incidence and number of mammary gland fibroadenomas were higher in group 6 ($p<0.05$ *vs.* control). Incidence of preneoplastic hepatic lesions was greater for groups 2 and 5 (eosinophilic foci) and group 3 (clear cell foci) at 100 weeks ($p<0.05$ *vs.* control). Non-neoplastic treatment effects included chronic progressive nephropathy (CPN), hepatocyte single-cell necrosis, and centrilobular hepatocyte hypertrophy at 52 weeks (groups 2 and 5) and CPN at 100 weeks (groups 2-5) ($p<0.05$ *vs.* control).

Discussion: Chronic DCA exposure did not increase hepatic tumorigenesis in female rats. Further work is needed to confirm DCA effects on mammary gland tumors and CPN.

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